Supplementary Appendix

This appendix has been provided by the authors to give readers additional information about their work.

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List of investigators

Investigator	Institution	Location
Olutola Adetona	Tekton Research - Texas - Platinum	San Antonio, Texas
Adebayo Akinsola	Tekton Research - Georgia - Platinum	Chamblee, Georgia
Kashif Ali	DM Clinical Research - Kool Kids Pediatrics	Houston, Texas
Madhavi Ampajwala	ACRC Trials - Hunt	Plano, Texas
Gary Berman	Clinical Research Institute, Inc	Minneapolis, Minnesota
Gary Boone	Paradigm Clinical Research	La Mesa, California
Robert Buynak	Velocity Clinical Research - Valparaiso	Valparaiso, Indiana
Quito Carr	MedPharmics, LLC. - Albuquerque	Albuquerque, New Mexico
Laurence Chu	Benchmark Research - Austin	Austin, Texas
Robert Clifford	Coastal Pediatric Associates	Charleston, South Carolina
Salma Elfaki	Accel Research Sites - Nona Pediatric Center	Orlando, Florida
Kenneth Etokhana	Tekton Research - Texas - Platinum	San Antonio, Texas
Carlos Fierro	Johnson County Clin-Trials	Lenexa, Kansas
Carl Griffin	Lynn Health Science Institute	Oklahoma City, Oklahoma
Robert Jeanfreau	MedPharmics - Platinum	Metairie, Louisiana
Judith Kirstein	Velocity Clinical Research - Banning	West Jordan, Utah
Paul Matherne	MedPharmics - Platinum	Gulfport, Mississippi
Richard Ohnmacht	Velocity Clinical Research - Providence	Warwick, Rhode Island
Paul Pickrell	Tekton Research - Texas - Platinum	Austin, Texas
Richard Powell	Velocity Clinical Research - Cincinnati	Cincinnati, Ohio
Celia Reyes-Acuna	Crossroads Clinical Research (Victoria)	Corpus Christi, Texas
Barbara Rizzardi	Velocity Clinical Research - Salt Lake City - Jordan Valley	West Jordan, Utah
Katherine Ruiz-de-Luzuriaga	University of Massachusetts Medical School	Worcester, Massachusetts
Nathan Segall	Clinical Research Atlanta	Stockbridge, Georgia
Mark Turner	Velocity Clinical Research - Boise	Meridiani Idaho
Leonard Weiner	Child Healthcare Associates - East Syracuse	Syracuse, New York

Supplementary Methods

Assessment of Noninferiority of Immunogenicity and Seroresponse

For the primary immunogenicity analysis, approximately 362 participants who received mRNA-1273 were selected for the immunogenicity subset, with a target of 289 participants in the PP immunogenicity subset (adjusted for approximately 20% of participants who may be excluded from the PP immunogenicity subset due to no immunogenicity results or any other reasons). Noninferiority tests of two null hypotheses based on two coprimary endpoints, respectively, were planned and the sample size calculation for each of the two noninferiority tests was performed, and the larger sample size was chosen for the study. With approximately 289 adolescents in the PP Immunogenicity Subsets in this study and 289 young adults (18- ≤25 years of age) in that of the phase 3 COVE trial, there was 90% power to demonstrate noninferiority of the immune response measured by nAb geometric mean titers (GMTs) in adolescents at a 2-sided alpha of 0.05, compared with that in young adults (18- ≤25 years of age) from the COVE study receiving mRNA-1273, assuming an underlying geometric mean ratio (GMR) value of 1 and a noninferiority margin of 1.5. The standard deviation (SD) of the log-transformed levels was assumed to be 1.5. With approximately 289 adolescents in the Per-protocol Immunogenicity Subsets in this study and 289 young adults (18- ≤25 years of age) in the phase 3 COVE trial, there would be at least 90% power to demonstrate noninferiority of the immune response as measured by the seroresponse rate in adolescents in this study at a 2-sided alpha of 0.05, compared with that in young adults (18-25 years of age) from the phase 3 COVE trial receiving mRNA-1273, assuming a true seroresponse rate of 85% in young adults (18- ≤25 years of age) from COVE and a true seroresponse rate of 85% in adolescents in this study (i.e., true rate difference is 0 compared to young adults from the phase 3 COVE trial), and a noninferiority margin of 10%.

The noninferiority of immune response to mRNA-1273 in adolescents compared to young adults was demonstrated by meeting the success criteria for both coprimary endpoints at Day 57: the lower bound of the 95% CI of the GMT ratio was > 0.67 based on the noninferiority margin of 1.5, and GMT ratio point estimate > 0.8 (minimum threshold); and the lower bound of the 95% of the seroresponse rate difference was > -10% based on the noninferiority margin of 10%, and the seroresponse rate difference point estimate > -5% (minimum threshold).

Selection of the immunogenicity subset

The first ~550 participants enrolled in the study were selected for the immunogenicity subset. This subset was considered representative of the overall study subjects, because demographics and baseline characteristics in this subset were similar to those in the Full Analysis Set, and the entire study enrollment completed within a short period of < 3 months (09 Dec 2020 – 28 Feb 2021) supporting the homogeneity of the early enrolled participants and those enrolled subsequently. The ~550 participants (including mRNA-1273 and placebo participants in a ratio of 2:1 to maintain treatment being blinded) in the FAS who had no Baseline SARS-CoV-2 missing data provided at least 362 recipients of mRNA-1273 in the immunogenicity subset from which at least 289 recipients of mRNA-1273 were expected to be obtained for the per-protocol (PP) immunogenicity subset for the primary immunogenicity analysis, assuming 20% to be excluded from the PP Set for baseline positive SAR-CoV-2 status, or have no immunogenicity results due to any reasons.. From the P301 COVE study, an immunogenicity subset (n=340 recipients of mRNA-1273) was randomly selected from the 18- ≤25 years of age group, from which ~289 participants were expected to be included in the PP immunogenicity subset, assuming 15% to be excluded from the PP set for any reasons. The PP immunogenicity subset included those in the immunogenicity subset who received planned injections of study vaccination and immunogenicity

blood sampling per schedule, with negative RT-PCR for SARS-CoV-2 and negative serology specific to SARS-CoV-2 nucleocapsid at baseline, and without major protocol deviations.

Safety assessment

Safety assessments included monitoring solicited local and systemic adverse reactions (ARs) that occurred during the 7 days following each injection daily by participants using eDiaries, unsolicited adverse events (AEs) observed or reported during the 28 days following each injection, AEs leading to discontinuation from dosing and/or withdrawal from study participation from Day 1 through the last day of study participation, medically attended adverse events (MAAEs) and serious AEs (SAEs) from first injection on day 1 through the entire study period. Adverse events of special interest (AESI) of multisystem inflammatory syndrome in children (MIS-C) vital sign measurements, physical examination findings, and assessments for SARS-CoV-2 infection were monitored from day 1 through study completion. Trained site personnel made telephone calls to the participants to assess safety every 4 weeks. Details of all pregnancies in female participants were collected after the start of study treatment and until the end of their participation in the study. Safety data are presented as descriptive summaries of counts, percentages and associated Clopper-Pearson 95% CIs.

There were 5 (0.4%) and 19 (0.8%) unsolicited AEs that were medically-attended and considered related to study vaccine up to 28 days after any injection in the placebo and mRNA-1273 groups, respectively (Table S3). None led to discontinuation from participation in the study (Table S3). The imbalance in treatment-emergent AEs considered related to mRNA-1273 (lymphadenopathy and headache) were manifestations of reactogenicity.

Assessment of efficacy

To evaluate the incidence of Covid-19, SARS-CoV-2 infection regardless of symptoms, and asymptomatic infection after vaccination with mRNA-1273 or placebo, the incidence rates were

provided by vaccination group, calculated as the number of cases divided by the total person-time. The incidence rate ratio of mRNA-1273 versus placebo was provided with its 95% CI computed using the exact method conditional upon the total number of cases adjusted by the total person-time. Person-time was defined as the total time from randomization date to the date of event, last date of study participation, censoring time, or efficacy data cutoff date, whichever is earlier. Vaccine efficacy was defined as 1 – ratio of incidence rate (mRNA-1273 vs. placebo).

Efficacy analyses was performed using the FAS, mITT1 and PP Set for Efficacy. The mITT1 Set was the primary analysis set for efficacy analysis of cases starting from 14 days after first injection, and PP Set for Efficacy was the primary analysis set used in the efficacy analyses for cases starting 14 days after second injection, unless otherwise specified. Participants were included in the treatment group in which they were randomized.

SARS-CoV-2 Spike-Pseudotyped Virus Neutralization Assay

The quantification of SARS-CoV-2 neutralizing antibodies utilizes lentivirus particles that express SARS-CoV-2 spike protein (Wuhan-Hu-1 isolate including D614G) on their surface and contain a firefly luciferase reporter gene for quantitative measurements of infection by relative luminescence units (RLU) (Shen X, Tang H, McDanal C, et al. SARS-CoV-2 variant B.1.1.7 is susceptible to neutralizing antibodies elicited by ancestral spike vaccines. Cell Host Microbe 2021;29:529-39 e3). The virus is applied to transduced 293T cells expressing high levels of ACE2 (293T/ACE2 cells), with or without pre-incubation with antibodies (control antibodies or serum samples); the presence of neutralizing antibodies reduces infection and results in lower RLUs. Serial dilution of antibodies or serum samples can be used to produce a injection-response curve. Neutralization is measured as the serum dilution at which the RLU is reduced by 50% (50 percent inhibitory injection [ID50]) or 80%

(80 percent inhibitory injection [ID80]) relative to mean RLU in virus control wells (cells + virus but no control antibody or sample) after subtraction of the mean RLU in cell control wells (cells only). Immune Assay Team at Duke University Medical Center: Rebecca Beerman, Kendall Bradley, Jiayu Chen, Xiaoju Daniell, Elizabeth Domin, Amanda Eaton, Kelsey Engle, Wenhong Feng, Juanfei Gao, Hongmei Gao, Kelli Greene, Sarah Hiles, Marianne Jessup-Cumming, Marcella Sarzotti-Kelsoe, Kristy Long, Kellen Lund, Kaia Lyons, Charlene McDanal, David C. Montefiori, Francesca Suman, Haili Tang, Jin Tong, Olivia Widman.

SARS-CoV-2 Meso-Scale Discovery 3-PLEX assay

This quantitative electrochemiluminescence (ECL) method is an indirect binding ECL method designed to detect SARS-CoV-2 antibodies (SARS-CoV-2 Spike (S; Wuhan-Hu-1 isolate including D614G), nucleocapsid (N), and receptor binding domain (RBD) antibodies) in human serum. The assay is based on the Meso-Scale Discovery (MSD) technology which employs capture molecule MULTI-SPOT® microtiter plates fitted with a series of electrodes. Using an MSD MESO Sector S 600 detection system, an electrical current is applied to the custom microtiter plates leading to a light emission by SULFO-TAGTM through a series of oxidation-reduction reactions involving ruthenium and tripropylamine (TPA). A plate reader measures the intensity of emitted light to provide quantitative measures of analytes in samples.

For this bioassay, a 10-spot custom SARS-CoV-2 3-PLEX plate coated with SARS-CoV-2 antigens (S [containing D614G], N, and RBD) is used. Anti-SARS-CoV-2 antibodies present in the test sample bind to the antigen coated plates and form an antibody-antigen complexes. These complexes are detected by adding SULFO-TAGTM-labeled antibodies, which bind to the antibody-antigen complexes. Addition of TPA in a buffer solution results in ECL that is measured in relative light units (RLU) using the MSD SECTOR S 600 Plate Reader. Antibody concentrations are determined by

interpolating their ECL response using the standard curve generated from a serially diluted reference standard.

SARS-CoV-2 S-2P IgG ELISA

Microtiter plates are coated with commercially available SARS-CoV-2 full-length spike glycoprotein [Wuhan-Hu-1 isolate including D614G], and serum containing the SARS-CoV-2 IgG antibody is added. Bound antigen-antibody complex is detected using purified goat anti-human IgG horseradish peroxidase conjugate. Color development occurs with the addition of 3,3′,5,5′tetramethylbenzidine substrate and color intensity is measured spectrophotometrically (450 nm). The intensity of the color is directly proportional to the IgG antibody concentration. Quantitation of the human IgG antibody to SARS-CoV-2, or antibody concentration (AU/mL), is determined by interpolation from a standard curve analyzed on each assay plate.

Table S1: Primary and Secondary Objectives and Endpoints

Primary or Secondary	Objective	Endpoint
Primary	To evaluate the safety and reactogenicity of 100 µg of mRNA-1273 administered in 2 injections 28 days apart	Solicited local and systemic adverse reactions through 7 days after each injection
Primary	To evaluate the safety and reactogenicity of 100 µg of mRNA-1273 administered in 2 injections 28 days apart	Unsolicited adverse events through 28 days after each injection
Primary	To infer efficacy of mRNA-1273 (100 µg, 2 injections 28 days apart), serum antibody responses obtained 28 days after the second injection of mRNA-1273 (Day 57) in adolescents (this clinical study) with those obtained from young adult recipients (18-25 years of age) of mRNA-1273 in the clinical endpoint efficacy trial (phase 3 COVE study)	Efficacy will be inferred based on establishing noninferiority of neutralizing antibody values and seroresponse rates in adolescents (12 to < 18 yrs; this clinical study) to values obtained from young adults (18-25 yrs) in the phase 3 COVE study (geometric mean value 12 to < 18 yrs / geometric mean value 18-25 yrs)
Secondary	To evaluate the incidence of Covid-19 starting 14 days after the second injection of mRNA-1273 or placebo.	Covid-19 is defined as symptomatic disease based on the following criteria: − at least TWO of the following systemic symptoms: fever (≥ 38ºC/≥ 100.4ºF), chills, myalgia, headache, sore throat, new olfactory and taste disorder(s), OR − at least ONE of the following respiratory signs/symptoms: cough, shortness of breath or difficulty breathing, OR clinical or radiographical evidence of pneumonia; AND − The participant must have at least 1 NP swab, nasal swab, or saliva sample (or respiratory sample, if hospitalized) positive for SARS-CoV-2 by RT-PCR
Secondary	Determine the incidence of the first occurrence of Covid-19 cases meeting the secondary case definition starting 14 days after the first injection of mRNA-1273, and Covid-19 cases starting 14 days after the second injection of mRNA-1273.	The secondary case definition of Covid-19 is defined by the following criteria: − One systemic or respiratory symptoms: fever (temperature > 38ºC/≥ 100.4ºF), or chills, cough, shortness of breath or difficulty breathing, fatigue, muscle aches, or body aches, headache, new loss of taste or smell, sore throat, congestion or runny nose, nausea, or vomiting or diarrhea, AND − At least one positive RT-PCR test for SARS CoV-2

Secondary	To evaluate the effect of mRNA-1273 on the incidence of SARS-CoV-2 infection (regardless of symptoms) compared with the incidence among placebo recipients.	A combination of Covid-19 and asymptomatic SARS-CoV-2 infection for participants with negative SARS-CoV-2 status at baseline: bAb levels against SARS-CoV-2 nucleocapsid protein negative (as measured by Roche Elecsys) at Day 1 that becomes positive (as measured by Roche Elecsys) counted starting at Day 57 or later, OR Positive RT-PCR test.
Secondary	Determine the incidence of asymptomatic SARS-CoV-2 infection measured by RT-PCR and/or serology tests obtained at post-baseline visits counted starting 14 days after the second injection in participants with negative SARS-COV-2 status at baseline.	Asymptomatic SARS-CoV-2 infection is identified by absence of symptoms and infections as detected by RT-PCR or serology tests. Specifically: − Absent of Covid-19 symptoms − AND at least one from below: − Binding antibody level against SARS-CoV-2 nucleocapsid protein negative (as measured by Roche Elecsys) at Day 1 that becomes positive (as measured by Roche Elecsys) counted starting at Day 57 or later, OR − Positive RT-PCR test at scheduled or unscheduled/illness visits

Figures

Figure S1. Analysis populations

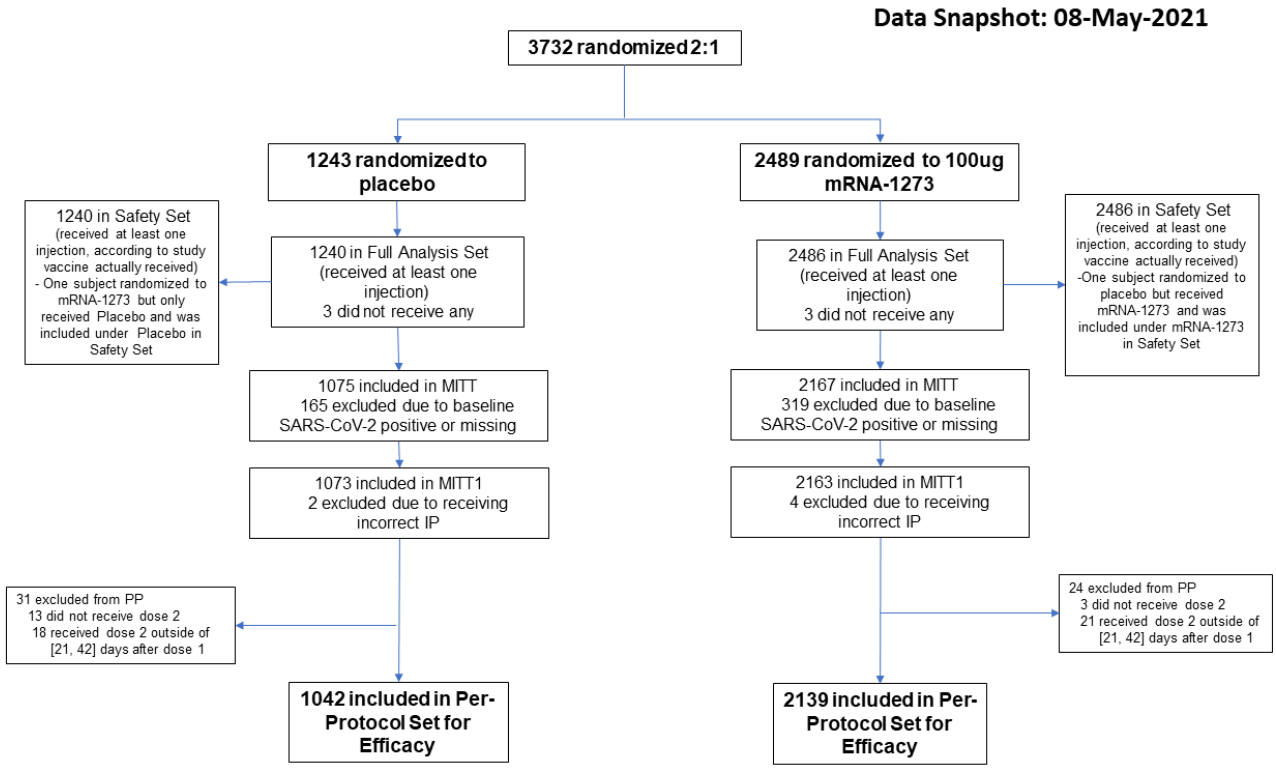


Figure S1. Analysis populations. Full analysis set=All randomized participants who received at least 1 injection; PP= Per-Protocol for Efficacy, all participants in the FAS who received planned injections of study vaccination, complied with the timing of injection 2, had no immunologic and virologic evidence of prior Covid-19 at baseline, and no major protocol deviations; mITT= Modified Intent-to-Treat Set, all participants in the FAS who had no serologic or virologic evidence of prior SARS-CoV-2 infection before the first injection (both negative RT-PCR test for SARS-CoV-2 and negative serology test based on bAb specific to SARS-CoV-2 nucleocapsid) at baseline; mITT1= all participants in the mITT Set excluding those who received the wrong treatment; Safety set= All randomized participants who received at least 1 injection; PP Immunogenicity set= A subset of participants in the FAS will be selected for immunogenicity testing. The PP Immunogenicity Subset included participants selected for the Immunogenicity Subset who received planned injections of study vaccination per schedule, complied with the timing of injection 2, had no immunologic and virologic evidence of prior Covid-19 at baseline, complied with immunogenicity testing schedule, and had no major protocol deviations that impacted key or critical data, participants who were seropositive at baseline were excluded from the PP Immunogenicity Subset.

Figure S2: Cumulative Incidence of CDC Definition of Covid-19 Starting 14 Days After First Injection – mITT1 Set

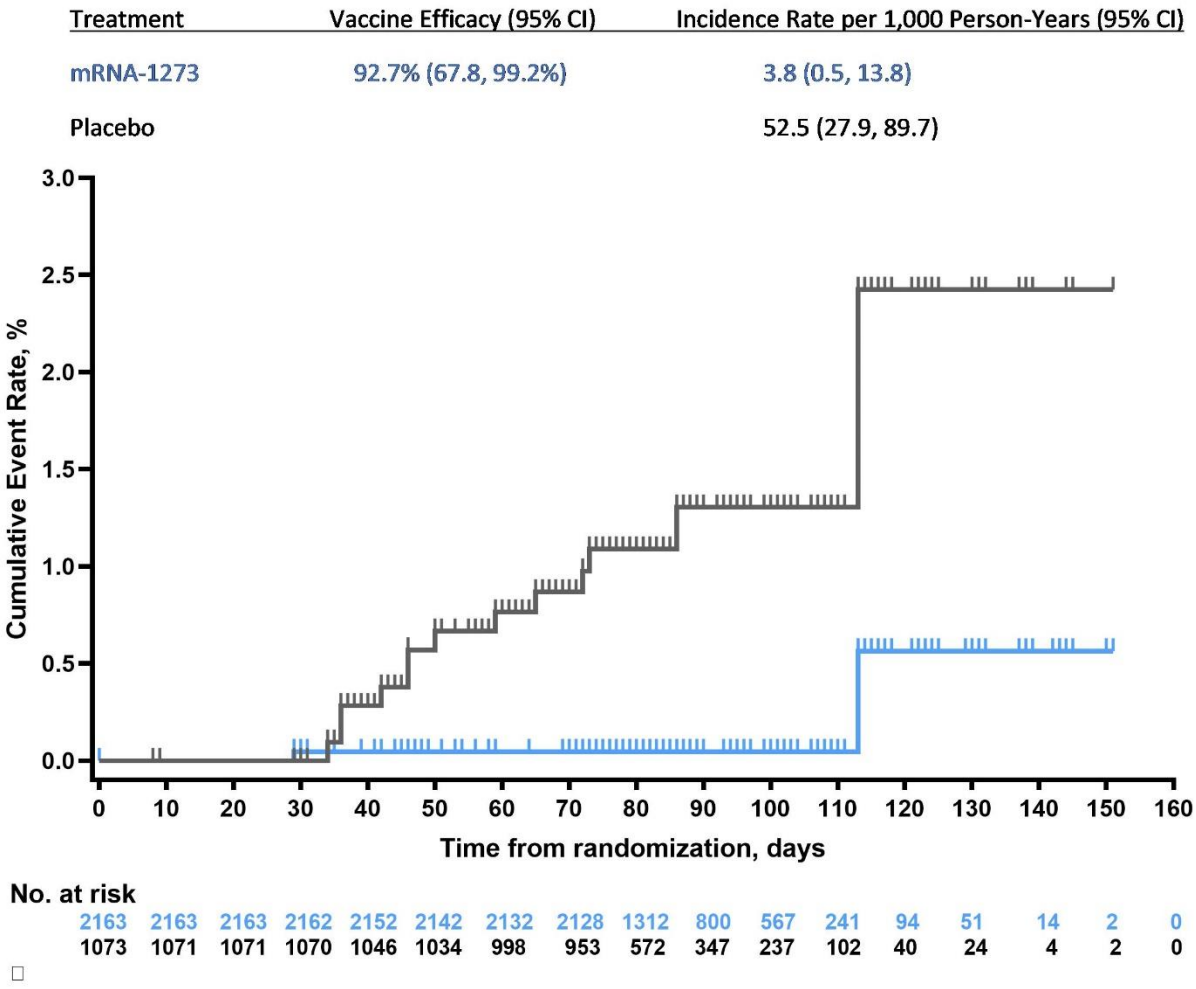


Figure S3: Pseudovirus Neutralizing Antibody ID50 Titers by Age Group

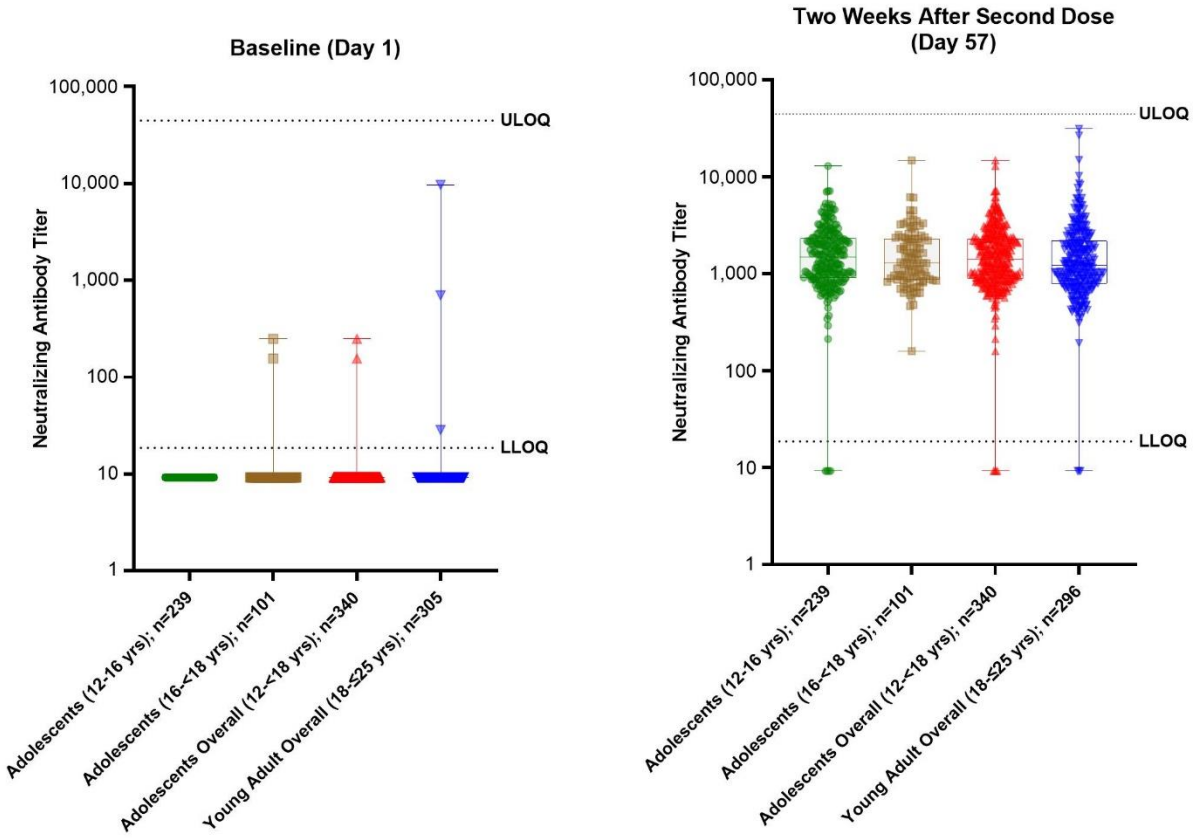
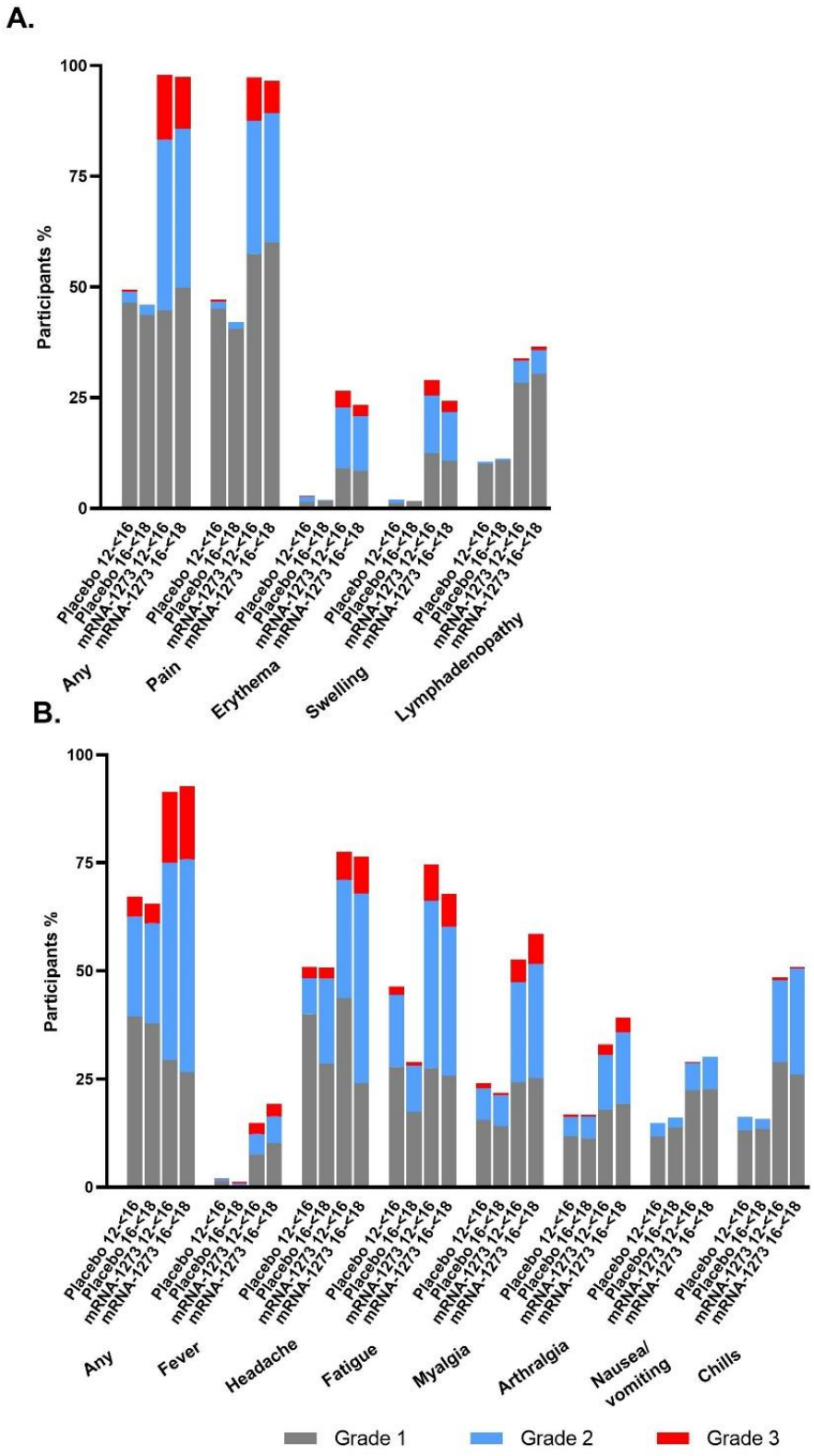


Figure S3: Pseudovirus Neutralizing Antibody ID50 Titers by Age Group. Boxes indicate interquartile ranges (IQR) from Q1 to Q3. The medians are shown by the lines within the boxes. The error bars are the minimum to maximum. Individual data points are shown by the symbols (circles; squares; triangles). Per-protocol Immunogenicity Subset; Lower limit of quantitation (LLOQ)= 18.5; Upper limit of quantitation (ULOQ)=45,118. Antibody values reported as below LLOQ were replaced by 0.5 x LLOQ. Values greater than ULOQ were replaced by the ULOQ if actual values were not available.

Figure S4: Solicited Adverse Reactions Within 7 Days After Any Injection by Age Group (12-<16; 16-<18 years)



Tables

Table S2: Solicited Local and Systemic Adverse Reactions within 7 Days After Each Injection

Adverse Reaction N (%)	First Injection			Second Injection		
	Placebo N=1238	mRNA-1273 N=2482	Total N=3720	Placebo N=1220	mRNA-1273 N=2478	Total N=3698
Solicited AR, N1	1238	2482	3720	1220	2478	3698
Any Solicited AR	806 (65.1)	2381 (95.9)	3187 (85.7)	680 (55.7)	2405 (97.1)	3085 (83.4)
Grade 1	576 (46.5)	1218 (49.1)	1794 (48.2)	470 (38.5)	775 (31.3)	1245 (33.7)
Grade 2	194 (15.7)	930 (37.5)	1124 (30.2)	181 (14.8)	1144 (46.2)	1325 (35.8)
Grade 3	36 (2.9)	233 (9.4)	269 (7.2)	28 (2.3)	483 (19.5)	511 (13.8)
Grade 4	0 (0)	0 (0)	0 (0)	1 (<0.1)	3 (0.1)	4 (0.1)
Any Solicited Local AR, N1	1238	2482	3720	1220	2478	3698
Any Solicited Local AR	455 (36.8)	2339 (94.2)	2794 (75.1)	398 (32.6)	2314 (93.4)	2712 (73.3)
Grade 1	441 (35.6)	1517 (61.1)	1958 (52.6)	373 (30.6)	1343 (54.2)	1716 (46.4)
Grade 2	13 (1.1)	652 (26.3)	665 (17.9)	22 (1.8)	751 (30.3)	773 (20.9)
Grade 3	1 (<0.1)	170 (6.8)	171 (4.6)	3 (0.2)	220 (8.9)	223 (6.0)
Grade 4	0	0	0	0	0	0
Local AR, Pain, N1	1238	2482	3720	1220	2478	3698
Pain	431 (34.8)	2310 (93.1)	2741 (73.7)	370 (30.3)	2290 (92.4)	2660 (71.9)
Grade 1	421 (34.0)	1676 (67.5)	2097 (56.4)	351 (28.8)	1595 (64.4)	1946 (52.6)
Grade 2	9 (0.7)	501 (20.2)	510 (13.7)	16 (1.3)	569 (23.0)	585 (15.8)
Grade 3	1 (<0.1)	133 (5.4)	134 (3.6)	3 (0.2)	126 (5.1)	129 (3.5)
Grade 4	0	0	0	0	0	0
Erythema, N1	1238	2482	3720	1220	2478	3698
Erythema	8 (0.6)	334 (13.5)	342 (9.2)	11 (0.9)	484 (19.5)	495 (13.4)
Grade 1	8 (0.6)	158 (6.4)	166 (4.5)	9 (0.7)	150 (6.1)	159 (4.3)
Grade 2	0	155 (6.2)	155 (4.2)	2 (0.2)	262 (10.6)	264 (7.1)
Grade 3	0	21 (0.8)	21 (0.6)	0	72 (2.9)	72 (1.9)
Grade 4	0	0	0	0	0	0
Swelling, N1	1238	2482	3720	1220	2478	3698
Swelling	12 (1.0)	403 (16.2)	415 (11.2)	12 (1.0)	509 (20.5)	521 (14.1)
Grade 1	9 (0.7)	228 (9.2)	237 (6.4)	8 (0.7)	214 (8.6)	222 (6.0)
Grade 2	3 (0.2)	148 (6.0)	151 (4.1)	4 (0.3)	239 (9.6)	243 (6.6)
Grade 3	0	27 (1.1)	27 (0.7)	0	56 (2.3)	56 (1.5)
Grade 4	0	0	0	0	0	0
Axillary Swelling, N1	1238	2482	3720	1220	2477	3697
Axillary Swelling	101 (8.2)	578 (23.3)	679 (18.3)	61 (5.0)	519 (21.0)	580 (15.7)
Grade 1	97 (7.8)	497 (20.0)	594 (16.0)	59 (4.8)	445 (18.0)	504 (13.6)
Grade 2	4 (0.3)	71 (2.9)	75 (2.0)	2 (0.2)	67 (2.7)	69 (1.9)
Grade 3	0	10 (0.4)	10 (0.3)	0	7 (0.3)	7 (0.2)
Grade 4	0	0	0	0	0	0
Any Systemic AR, N1	1238	2482	3720	1220	2478	3698
Any Systemic AR	687 (55.5)	1701 (68.5)	2388 (64.2)	561 (46.0)	2134 (86.1)	2695 (72.9)
Grade 1	461 (37.2)	957 (38.6)	1418 (38.1)	358 (29.3)	745 (30.1)	1103 (29.8)
Grade 2	190 (15.3)	636 (25.6)	826 (22.2)	177 (14.5)	1046 (42.2)	1223 (33.1)

Grade 3	36 (2.9)	108 (4.4)	144 (3.9)	25 (2.0)	340 (13.7)	365 (9.9)
Grade 4	0	0	0	1 (<0.1)	3 (0.1)	4 (0.1)
Fever, N1	1238	2480	3718	1219	2477	3696
Fever	12 (1.0)	63 (2.5)	75 (2.0)	12 (1.0)	302 (12.2)	314 (8.5)
Grade 1	9 (0.7)	36 (1.5)	45 (1.2)	6 (0.5)	162 (6.5)	168 (4.5)
Grade 2	2 (0.2)	18 (0.7)	20 (0.5)	4 (0.3)	93 (3.8)	97 (2.6)
Grade 3	1 (<0.1)	9 (0.4)	10 (0.3)	1 (<0.1)	46 (1.9)	47 (1.3)
Grade 4	0	0	0	1 (<0.1)	1 (<0.1)	2 (<0.1)
Headache, N1	1238	2480	3718	1220	2478	3698
Headache	477 (38.5)	1106 (44.6)	1583 (42.6)	370 (30.3)	1739 (70.2)	2109 (57.0)
Grade 1	400 (32.3)	821 (33.1)	1221 (32.8)	299 (24.5)	1007 (40.6)	1306 (35.3)
Grade 2	60 (4.8)	229 (9.2)	289 (7.8)	57 (4.7)	619 (25.0)	676 (18.3)
Grade 3	17 (1.4)	56 (2.3)	73 (2.0)	14 (1.1)	112 (4.5)	126 (3.4)
Grade 4	0	0	0	0	1 (<0.1)	1 (<0.1)
Fatigue, N1	1238	2481	3719	1220	2478	3698
Fatigue	453 (36.6)	1188 (47.9)	1641 (44.1)	353 (28.9)	1679 (67.8)	2032 (54.9)
Grade 1	299 (24.2)	683 (27.5)	982 (26.4)	212 (17.4)	639 (25.8)	851 (23.0)
Grade 2	136 (11.0)	472 (19.0)	608 (16.3)	131 (10.7)	852 (34.4)	983 (26.6)
Grade 3	18 (1.5)	33 (1.3)	51 (1.4)	10 (0.8)	188 (7.6)	198 (5.4)
Grade 4	0	0	0	0	0	0
Myalgia, N1	1238	2480	3718	1220	2477	3697
Myalgia	205 (16.6)	668 (26.9)	873 (23.5)	153 (12.5)	1154 (46.6)	1307 (35.4)
Grade 1	148 (12.0)	408 (16.5)	556 (15.0)	94 (7.7)	527 (21.3)	621 (16.8)
Grade 2	47 (3.8)	236 (9.5)	283 (7.6)	56 (4.6)	498 (20.1)	554 (15.0)
Grade 3	10 (0.8)	24 (1.0)	34 (0.9)	3 (0.2)	129 (5.2)	132 (3.6)
Grade 4	0	0	0	0	0	0
Arthralgia, N1	1238	2480	3718	1220	2477	3697
Arthralgia	143 (11.6)	371 (15.0)	514 (13.8)	113 (9.3)	716 (28.9)	829 (22.4)
Grade 1	107 (8.6)	252 (10.2)	359 (9.7)	78 (6.4)	370 (14.9)	448 (12.1)
Grade 2	31 (2.5)	104 (4.2)	135 (3.6)	33 (2.7)	289 (11.7)	322 (8.7)
Grade 3	5 (0.4)	15 (0.6)	20 (0.5)	2 (0.2)	57 (2.3)	59 (1.6)
Grade 4	0	0	0	0	0	0
Nausea/ vomiting, N1	1238	2480	3718	1220	2477	3697
Nausea / vomiting	110 (8.9)	281 (11.3)	391 (10.5)	106 (8.7)	591 (23.9)	697 (18.9)
Grade 1	97 (7.8)	238 (9.6)	335 (9.0)	81 (6.6)	452 (18.2)	533 (14.4)
Grade 2	13 (1.1)	41 (1.7)	54 (1.5)	25 (2.0)	136 (5.5)	161 (4.4)
Grade 3	0	2 (<0.1)	2 (<0.1)	0	2 (<0.1)	2 (<0.1)
Grade 4	0	0	0	0	1 (<0.1)	1 (<0.1)
Chills, N1	1238	2480	3718	1220	2477	3697
Chills	138 (11.1)	456 (18.4)	594 (16.0)	97 (8.0)	1066 (43.0)	1163 (31.5)
Grade 1	116 (9.4)	343 (13.8)	459 (12.3)	80 (6.6)	613 (24.7)	693 (18.7)
Grade 2	21 (1.7)	109 (4.4)	130 (3.5)	17 (1.4)	442 (17.8)	459 (12.4)
Grade 3	1 (<0.1)	4 (0.2)	5 (0.1)	0	11 (0.4)	11 (0.3)
Grade 4	0	0	0	0	0	0

N1=Number of exposed participants who submitted any data for the event.

Percentages based on the number of exposed participants who submitted any data for the event.

Table S3: Unsolicited Adverse Events up to 28 days after any Injection

	Placebo (N=1240) n (%)	mRNA-1273 (N=2486) n (%)	Total (N=3726) n (%)
Unsolicited AEs regardless of relationship to study vaccination			
All	197 (15.9)	510 (20.5)	707 (19.0)
Serious	1 (<0.1)	2 (<0.1)	3 (<0.1)
Fatal	0	0	0
Medically-attended	81 (6.5)	156 (6.3)	237 (6.4)
Leading to discontinuation from study vaccine	0	0	0
Leading to discontinuation from participation in the study	0	1 (<0.1)	1 (<0.1)
Severe	1 (<0.1)	4 (0.2)	5 (0.1)
Special interest of MIS-C	0	0	0
Unsolicited AEs related to study vaccination			
All	72 (5.8)	312 (12.6)	384 (10.3)
Serious	0	0	0
Fatal	0	0	0
Medically-attended	5 (0.4)*	19 (0.8)†	24 (0.6)
Leading to discontinuation from study vaccine	0	0	0
Leading to discontinuation from participation in the study	0	0	0
Severe	0	0	0
Special interest of MIS-C	0	0	0
Incidence of Unsolicited AEs up to 28 Days After Any Injection			
Lymphadenapathy	5 (0.4)	108 (4.3)	113 (3.0)
Headache	28 (2.3)	60 (2.4)	88 (2.4)

Unsolicited Adverse Events up to 28 days after any injection defined as any event not present before exposure to study vaccination or any event already present that worsens in intensity or frequency after exposure. Percentages are based on overall safety set.

* Five participants reported unsolicited treatment-related medically-attended adverse events [number of events] (nervous system disorder [1], respiratory, thoracic and mediastinal disorders [3], gastrointestinal disorder [1], musculoskeletal and connective tissue disorders [1], general disorders and administrative site conditions [3]).

† Nineteen participants reported unsolicited treatment-related medically-attended adverse events [number of events] (infections and infestations [1], blood and lymphatic system disorders [3], immune system disorders [1], psychiatric disorders [1], nervous system disorders [2], eye disorders [1], cardiac disorders [1], respiratory, thoracic and mediastinal disorders [2], gastrointestinal disorders [2], skin and subcutaneous tissue disorders [3], general disorders and administrative site conditions [5]).

Table S4: Number of Days Reporting Solicited Adverse Reactions

Adverse Reaction Mean (SD)	First Injection			Second Injection		
	Placebo N=1238	mRNA-1273 N=2482	Total N=3720	Placebo N=1220	mRNA-1273 N=2478	Total N=3698
Any Solicited	3.1 (3.5)	3.9 (3.5)	3.7 (3.5)	2.7 (3.8)	3.7 (3.5)	3.5 (3.6)
Any Local	2.0 (1.9)	3.3 (3.1)	3.1 (3.0)	2.0 (4.5)	3.2 (2.8)	3.0 (3.1)
Local						
Pain	1.8 (1.8)	2.8 (1.3)	2.6 (1.4)	1.9 (4.6)	2.9 (1.6)	2.7 (2.3)
Erythema	1.6 (1.8)	2.3 (1.8)	2.3 (1.8)	1.5 (0.9)	2.1 (2.9)	2.1 (2.8)
Swelling	1.8 (2.3)	2.2 (1.8)	2.2 (1.8)	2.3 (3.0)	2.3 (3.8)	2.3 (3.8)
Axillary Swelling	1.9 (1.5)	3.1 (5.3)	2.9 (4.9)	2.0 (1.2)	2.5 (3.3)	2.4 (3.2)
Any Systemic	3.1 (3.7)	2.9 (2.6)	2.9 (3.0)	2.5 (2.1)	2.8 (2.7)	2.7 (2.6)
Fever	1.3 (0.7)	1.2 (0.5)	1.2 (0.5)	1.4 (0.7)	1.2 (0.5)	1.2 (0.5)
Headache	2.3 (2.3)	2.2 (2.1)	2.3 (2.1)	2.2 (1.8)	2.3 (2.0)	2.3 (2.0)
Fatigue	2.5 (3.7)	2.4 (2.3)	2.4 (2.7)	2.2 (1.9)	2.2 (1.6)	2.2 (1.7)
Myalgia	2.4 (2.7)	2.1 (2.2)	2.2 (2.3)	2.0 (1.5)	1.8 (1.3)	1.8 (1.3)
Arthralgia	2.1 (1.7)	2.1 (2.5)	2.1 (2.3)	1.8 (1.3)	1.8 (1.5)	1.8 (1.5)
Nausea / vomiting	2.0 (4.1)	1.6 (1.6)	1.7 (2.6)	1.7 (1.4)	1.5 (1.2)	1.5 (1.3)
Chills	2.0 (1.8)	1.6 (2.0)	1.7 (2.0)	1.7 (1.2)	1.5 (2.6)	1.5 (2.6)

Percentages are based on the number of exposed participants who submitted any data for the event.

Table S5: Summary of Participants with Solicited Local Adverse Reactions Persisting Beyond Day 7 After or with Onset 7 Days After First and Second Injections

Adverse Reaction Persisting Beyond Day 7 n (%)	First Injection			Second Injection		
	Placebo N=1238	mRNA-1273 N=2482	Total N=3720	Placebo N=1220	mRNA-1273 N=2478	Total N=3698
Any Solicited Local AR	15 (1.2)	160 (6.4)	175 (4.7)	9 (0.7)	40 (1.6)	49 (1.3)
Grade 1	14 (1.1)	105 (4.2)	119 (3.2)	8 (0.7)	20 (0.8)	28 (0.8)
Grade 2	1 (<0.1)	49 (2.0)	50 (1.3)	1 (<0.1)	14 (0.6)	15 (0.4)
Grade 3	0	6 (0.2)	6 (0.2)	0	6 (0.2)	6 (0.2)
Grade 4	0	0	0	0	0	0
Local AR						
Pain	8 (0.6)	20 (0.8)	28 (0.8)	6 (0.5)	11 (0.4)	17 (0.5)
Grade 1	7 (0.6)	7 (0.3)	14 (0.4)	5 (0.4)	4 (0.2)	9 (0.2)
Grade 2	1 (<0.1)	11 (0.4)	12 (0.3)	1 (<0.1)	6 (0.2)	7 (0.2)
Grade 3	0	2 (<0.1)	2 (<0.1)	0	1 (<0.1)	1 (<0.1)
Grade 4	0	0	0	0	0	0
Erythema	1 (<0.1)	15 (0.6)	16 (0.4)	1 (<0.1)	6 (0.2)	7 (0.2)
Grade 1	1 (<0.1)	6 (0.2)	7 (0.2)	1 (<0.1)	0	1 (<0.1)
Grade 2	0	7 (0.3)	7 (0.2)	0	2 (<0.1)	2 (<0.1)
Grade 3	0	2 (<0.1)	2 (<0.1)	0	4 (0.2)	4 (0.1)
Grade 4	0	0	0	0	0	0
Swelling	1 (<0.1)	18 (0.7)	19 (0.5)	2 (0.2)	6 (0.2)	8 (0.2)
Grade 1	1 (<0.1)	6 (0.2)	7 (0.2)	2 (0.2)	1 (<0.1)	3 (<0.1)
Grade 2	0	9 (0.4)	9 (0.2)	0	5 (0.2)	5 (0.1)
Grade 3	0	3 (0.1)	3 (<0.1)	0	0	0
Grade 4	0	0	0	0	0	0
Axillary Swelling	7 (0.6)	127 (5.1)	134 (3.6)	1 (<0.1)	27 (1.1)	28 (0.8)
Grade 1	7 (0.6)	96 (3.9)	103 (2.8)	1 (<0.1)	20 (0.8)	21 (0.6)
Grade 2	0	28 (1.1)	28 (0.8)	0	6 (0.2)	6 (0.2)
Grade 3	0	3 (0.1)	3 (<0.1)	0	1 (<0.1)	1 (<0.1)
Grade 4	0	0	0	0	0	0
Adverse Reaction with Onset After Day 7 after any Injection n (%)	Placebo N=1240	mRNA-1273 N=2486	Total N=3726			
Any Solicited Local AR	0	32 (1.3)	32 (0.9)	-	-	-
Pain	0	6 (0.2)	6 (0.2)	-	-	-
Erythema	0	17 (0.7)	17 (0.5)	-	-	-
Swelling	0	11 (0.4)	11 (0.3)	-	-	-
Axillary swelling	0	11 (0.4)	11 (0.3)	-	-	-
Any Solicited Systemic AR	4 (0.3)	18 (0.7)	22 (0.6)	-	-	-
Fever	1 (<0.1)	4 (0.2)	5 (0.1)	-	-	-
Headache	2 (0.2)	7 (0.3)	9 (0.2)	-	-	-
Fatigue	2 (0.2)	8 (0.3)	10 (0.3)	-	-	-
Myalgia	0	4 (0.2)	4 (0.1)	-	-	-
Arthralgia	0	2 (<0.1)	2 (<0.1)	-	-	-
Nausea/Vomiting	1 (<0.1)	4 (0.2)	5 (0.1)	-	-	-
Chills	1 (<0.1)	1 (<0.1)	2 (<0.1)	-	-	-
Number of exposed participants who submitted any data for the event.						

Table S6: Analysis of Binding Antibody to SARS CoV-2 Spike Protein

	Adolescents 12 to <18 yrs n=340	**Young Adults 18 to ≤25 yrs n=280**	**Geometric Mean Ratio**
MSD antibody, (GM)	331,274	257,131	1.29
95% Confidence Interval	295,993-370,761	227, 124-291,103	1.09-1.52
	Adolescents 12 to <18 yrs n=340	**Young Adults 18 to ≤25 yrs n=295**	**Geometric Mean Ratio**
ELISA antibody, (GM)	807	740	1.09
95% Confidence Interval	730-892	664-824	0.94-1.26

Geometric Mean (GM) Ratio is for Adolescents vs. Young Adults; Antibody levels were measured by MSD or ELISA ; MSD=meso scale discovery; ELISA=enzyme-linked immunosorbent assay; Per-Protocol Immunogenicity Subset

Table S7: Secondary Efficacy Endpoints

Secondary Endpoint	Number of Cases		Person-years of follow-up		Incidence per 1000 person-years (95% CI)		Vaccine Efficacy (95% CI)
	Placebo	mRNA-1273	Placebo	mRNA-1273	Placebo	mRNA-1273	
Incidence of Covid-19* starting 14 days after second injection of mRNA-1273 in PP set	4	0	242.1	516.0	16.5 (4.5-42.3)	0.0 (NE-7.1)	100 (28.9-NE)
Incidence of Covid-19 (secondary definition)† starting 14 days after second injection of mRNA-1273 in PP set	7	1	241.5	515.7	29.0 (11.7-59.7)	1.9 (0.05-10.8)	93.3 (47.9-99.9)
Incidence of Covid-19 (secondary definition)† starting 14 days after first injection of mRNA-1273 in mITT1 set	13	2	247.7	522.4	52.5 (27.9-89.7)	3.8 (0.5-13.8)	92.7 (67.8-99.2)
Incidence of SARS-CoV-2 infection‡ starting 14 days after second injection of mRNA-1273 in PP set	23	22	238.0	513.3	96.6 (61.3-145.0)	42.9 (26.9- 64.9)	55.7 (16.8-76.4)
Incidence of SARS-CoV-2 infection‡ starting 14 days after first injection of mRNA-1273 in mITT1 set	42	27	244.0	520.0	172.1 (124.0-232.7)	51.9 (34.2-75.5)	69.8 (49.9-82.1)
Incidence of asymptomatic SARS-CoV-2 infection§ starting 14 days after second injection of mRNA-1273 in PP set	16	21	238.0	513.3	67.2 (38.4-1098.2)	40.9 (25.3- 62.5)	39.2 (-24.7-69.7)
Incidence of asymptomatic SARS-CoV-2 infection§ starting 14 days after first injection of mRNA-1273 in mITT1 set	29	25	244.0	520.0	118.8 (79.6-170.7)	48.1 (31.1- 71.0)	59.5 (28.4-77.3)

Table S7: Vaccine efficacy was calculated as 1 minus the ratio of incidence rate per 1,000 person years (mRNA-1273 vs. placebo). Person-years is defined as the total years from randomization date to the first date of COVID-19, SARS-CoV-2 infection, asymptomatic SARS-CoV-2 infection, last date of study participation, efficacy data cutoff/extraction date, or unblinding point, whichever is earlier.

*Covid-19 was defined as symptomatic disease based on criteria of a positive post-baseline RT-PCR test result AND at least two of the following systemic symptoms: fever (≥38ºC/≥100.4ºF), chills, myalgia, headache, sore throat, new olfactory and taste disorder(s); OR at least one of the following respiratory signs/symptoms: cough, shortness of breath or difficulty breathing, or clinical or radiographical evidence of pneumonia.

†Secondary case Covid-19 was defined as one of the following symptoms: fever (temperature > 38°C/≥ 100.4°F), or chills, cough, shortness of breath or difficulty breathing, fatigue, muscle aches, or body aches, headache, new loss of taste or smell, sore throat, congestion or runny nose, nausea, or vomiting or diarrhea AND a positive nasopharyngeal swab or saliva sample for SARS-CoV-2 by RT-PCR.

‡SARS-CoV-2 Infection (regardless of symptoms): A combination of Covid-19 and asymptomatic SARS-CoV-2 infection for participants with negative SARS-CoV-2 status at baseline – binding antibody levels against SARS-CoV-2 nucleocapsid protein negative (as measured by Roche Elecsys) at Day 1 that becomes positive (as measured by Roche Elecsys) counted starting at Day 57 or later, OR Positive RT-PCR test.

§ Asymptomatic SARS-CoV-2 infection is identified by absence of symptoms and infections as detected by RT-PCR or serology tests: Absent of Covid-19 symptoms AND at least one of the following: bAb level against SARS-CoV-2 nucleocapsid protein negative (as

measured by Roche Elecsys) at Day 1 that becomes positive (as measured by Roche Elecsys) counted starting at Day 57 or later, OR Positive RT-PCR test at scheduled or unscheduled/illness visits.

NE=Not estimated; PP= Per-Protocol for Efficacy, all participants who received at least one injection and received planned injections of study vaccination, complied with the timing of injection 2, had no immunologic and virologic evidence of prior Covid-19 at baseline, and no major protocol deviations, N=1042 (placebo), N=2139 (mRNA-1273); mITT1= all participants who had no serologic or virologic evidence of prior SARS-CoV-2 infection before the first injection (both negative RT-PCR test for SARS-CoV-2 and negative serology test based on binding antibody specific to SARS-CoV-2 nucleocapsid) at baseline, and excluding those who received the wrong treatment, N=1073 (placebo), N=2163 (mRNA-1273).

Table S8: Frequency of Solicited Local and Systemic Adverse Reactions Within 7 Days After First and Second Injections by Grade – Participants 12 to <18 Years of Age and Participants 18 to 25 Years of Age

Event	Injection 1*				Injection 2*			
	Study P203 12 to <18 Years	Study P301 18 to ≤25 Years	Study P203 12 to <18 Years	Study P301 18 to ≤25 Years	Study P203 12 to <18 Years	Study P301 18 to ≤25 Years	Study P203 12 to <18 Years	Study P301 18 to ≤25 Years
	mRNA-1273 N = 2482 (%)	mRNA-1273 N = 878 n (%)	Placebo N = 1238 n (%)	Placebo N = 900 n (%)	mRNA-1273 N = 2478 n (%)	mRNA-1273 N = 819 n (%)	Placebo N = 1220 n (%)	Placebo N = 839 n (%)
Any local adverse reaction, n	2,482	878	1,238	900	2,478	819	1,220	839
Any, n (%)	2,339 (94.2)	793 (90.3)	455 (36.8)	242 (26.9)	2,314 (93.4)	739 (90.2)	398 (32.6)	208 (24.8)
Grade 3, n (%)	170 (6.8)	52 (5.9)	1 (<0.1)	2 (0.2)	220 (8.9)	63 (7.7)	3 (0.2)	0
Grade 4, n (%)	0	0	0	0	0	0	0	0
Pain, n	2,482	878	1,238	900	2,478	819	1,220	839
Any	2,310 (93.1)	785 (89.4)	431 (34.8)	213 (23.7)	2,290 (92.4)	732 (89.4)	370 (30.3)	187 (22.3)
Grade 3†, n (%)	133 (5.4)	47 (5.4)	1 (<0.1)	2 (0.2)	126 (5.1)	53 (6.5)	3 (0.2)	0
Grade 4†, n (%)	0	0	0	0	0	0	0	0
Erythema (redness), n	2,482	878	1,238	900	2,478	819	1,220	839
Any, n (%)	334 (13.5)	33 (3.8)	8 (0.6)	6 (0.7)	484 (19.5)	60 (7.3)	11 (0.9)	3 (0.4)
Grade 3‡, n (%)	21 (0.8)	2 (0.2)	0	0	72 (2.9)	7 (0.9)	0	0
Grade 4‡, n (%)	0	0	0	0	0	0	0	0
Swelling (hardness), n	2,482	878	1,238	900	2,478	819	1,220	839
Any, n (%)	403 (16.2)	71 (8.1)	12 (1.0)	5 (0.6)	509 (20.5)	83 (10.1)	12 (1.0)	3 (0.4)
Grade 3‡, n (%)	27 (1.1)	5 (0.6)	0	0	56 (2.3)	8 (1.0)	0	0
Grade 4‡, n (%)	0	0	0	0	0	0	0	0
Axillary swelling or tenderness, n	2,481	878	1,238	900	2,477	819	1,220	839
Any, n (%)	578 (23.3)	160 (18.2)	101 (8.2)	71 (7.9)	519 (21.0)	153 (18.7)	61 (5.0)	48 (5.7)
Grade 3d, n (%)	10 (0.4)	2 (0.2)	0	0	7 (0.3)	3 (0.4)	0	0
Grade 4d, n (%)	0	0	0	0	0	0	0	0

Any systemic AR, n	2,482	878	1,238	900	2,478	819	1,220	839
Any, n (%)	1,701 (68.5)	578 (65.8)	687 (55.5)	486 (54.0)	2,134 (86.1)	702 (85.7)	561 (46.0)	343 (40.9)
Grade 3, n (%)	108 (4.4)	46 (5.2)	36 (2.9)	26 (2.9)	340 (13.7)	177 (21.6)	25 (2.0)	23 (2.7)
Grade 4, n (%)	0	0	0	0	3 (0.1)	0	1 (<0.1)	0
Fever, n	2,480	878	1,238	899	2,477	819	1,219	839
Any, n (%)	63 (2.5)	15 (1.7)	12 (1.0)	5 (0.6)	302 (12.2)	149 (18.2)	12 (1.0)	1 (0.1)
Grade 3[†], n (%)	9 (0.4)	0	1 (<0.1)	0	46 (1.9)	10 (1.2)	1 (<0.1)	0
Grade 4[†], n (%)	0	0	0	0	1 (<0.1)	0	1 (<0.1)	0
Headache, n	2,480	878	1,238	900	2,478	819	1,220	839
Any, n (%)	1,106 (44.6)	376 (42.8)	477 (38.5)	314 (34.9)	1,739 (70.2)	574 (70.1)	370 (30.3)	222 (26.5)
Grade 3[‡], n (%)	56 (2.3)	28 (3.2)	17 (1.4)	14 (1.6)	112 (4.5)	52 (6.3)	14 (1.1)	11 (1.3)
Grade 4[‡], n (%)	0	0	0	0	1 (<0.1)	0	0	0
Fatigue	2,481	878	1,238	900	2,478	819	1,220	839
Any, n (%)	1,188 (47.9)	403 (45.9)	453 (36.6)	330 (36.7)	1,679 (67.8)	567 (69.2)	353 (28.9)	242 (28.8)
Grade 3[§], n (%)	33 (1.3)	13 (1.5)	18 (1.5)	12 (1.3)	188 (7.6)	96 (11.7)	10 (0.8)	11 (1.3)
Grade 4[§], n (%)	0	0	0	0	0	0	0	0
Myalgia, n	2,480	878	1,238	900	2,477	819	1,220	839
Any, n (%)	668 (26.9)	249 (28.4)	205 (16.6)	134 (14.9)	1,154 (46.6)	490 (59.8)	153 (12.5)	112 (13.3)
Grade 3[§], n (%)	24 (1.0)	12 (1.4)	10 (0.8)	4 (0.4)	129 (5.2)	92 (11.2)	3 (0.2)	4 (0.5)
Grade 4[§], n (%)	0	0	0	0	0	0	0	0
Arthralgia, n	2,480	878	1,238	900	2,477	819	1,220	839
Any, n (%)	371 (15.0)	154 (17.5)	143 (11.6)	98 (10.9)	716 (28.9)	340 (41.5)	113 (9.3)	67 (8.0)
Grade 3[§], n (%)	15 (0.6)	5 (0.6)	5 (0.4)	0	57 (2.3)	47 (5.7)	2 (0.2)	4 (0.5)
Grade 4[§], n (%)	0	0	0	0	0	0	0	0
Nausea/vomiting, n	2,480	878	1,238	900	2,477	819	1,220	839
Any, n (%)	281 (11.3)	113 (12.9)	110 (8.9)	98 (10.9)	591 (23.9)	231 (28.2)	106 (8.7)	80 (9.5)
Grade 3[‖], n (%)	2 (<0.1)	0	0	1 (0.1)	2 (<0.1)	0	0	2 (0.2)
Grade 4[‖], n (%)	0	0	0	0	1 (<0.1)	0	0	0
Chills, n	2,480	878	1,238	900	2,477	819	1,220	839

Any, n (%)	456 (18.4)	126 (14.4)	138 (11.1)	75 (8.3)	1,066 (43.0)	431 (52.6)	97 (8.0)	66 (7.9)
Grade 3[¶], n (%)	4 (0.2)	0	1 (<0.1)	0	11 (0.4)	11 (1.3)	0	1 (0.1)
Grade 4[¶], n (%)	0	0	0	0	0	0	0	0

Abbreviations: Any = grade 1 or higher; eDiary = electronic diary; N = number of exposed participants in the safety set; n = number of exposed participants who submitted any data for the event; SAR = solicited adverse reaction.
Note: Percentages are based on the number of exposed participants who submitted any data for the event (N1). The Solicited Safety Set consists of all participants who were randomized and received at least 1 injection of IP and contributed any solicited AR data (i.e., had at least 1 postbaseline solicited safety assessment). The First (Second) Injection Solicited Safety Set consists of all participants in the Solicited Safety Set who received the first (second) injection and contributed any solicited AR data from the time of the first (second) injection through the following 6 days. Medications were collected on the eDiary.
[*] The First and Second Injection Solicited Safety Set consist of all participants in the Solicited Safety Set who received injection 1 or 2 and contributed any SAR data (eDiary) from the time of injection 1 or 2 through the following 6 days.
[†] Fever is defined as: Grade 3 = 39 to 40°C; Grade 4 = greater than 40°C.
[‡]Headache: Grade 3 significant, any use of prescription pain reliever or prevents daily activity; Grade 4 requires emergency room visit or hospitalization.
[§]Fatigue, myalgia, arthralgia: Grade 3 significant, prevents daily activity; Grade 4 requires emergency room visit or hospitalization.
[‖]Nausea/vomiting: Grade 3 prevents daily activity, requires outpatient intravenous hydration; Grade 4 requires emergency room visit or hospitalization for hypotensive shock.
[¶]Chills: Grade 3 prevents daily activity and requires medical intervention; Grade 4 requires emergency room visit or hospitalization.

Table S9: Serious Adverse Events by System Organ Class and Preferred Term in Safety Set

System Organ Class (Preferred Term)	Placebo (N=1240) n (%)	mRNA-1273 (N=2486) n (%)
Number of Participants Reporting Unsolicited Adverse Events	2 (0.2)	6 (0.2)
Number of Unsolicited Adverse Events	2	9
Infections and infestations		
Appendicitis	0	1 (<0.1)
Psychiatric disorders	1 (<0.1)	3 (0.1)
Suicidal ideation	0	2 (<0.1)
Depression suicidal	0	1 (<0.1)
Suicide attempt	1 (<0.1)	0
Gastrointestinal disorders	0	1 (<0.1)
Diarrhea	0	1 (<0.1)
Vomiting	0	1 (<0.1)
Hepatobiliary disorders	0	1 (<0.1)
Drug-induced liver injury	0	1 (<0.1)
Renal and urinary disorders	1 (<0.1)	0
Obstructive nephropathy	1 (<0.1)	0
Congenital, familial and genetic disorders	0	1 (<0.1)
Pectus excavatum	0	1 (<0.1)
Injury, poisoning and procedural complications	0	1 (<0.1)
Post procedural fever	0	1 (<0.1)

Percentages are based on the number of participants in the Safety Set (N).

Table S10: Demographic and Baseline Characteristics in Per-Protocol Immunogenicity Subset for Participants Aged 12 to <18 Years and Participants Aged 18 to ≤25 Years)

Characteristic	12 to <18 yrs (N = 340) n (%)	18 to ≤25 yrs (N = 305) n (%)
Sex		
Female	162 (47.6)	157 (51.5)
Male	178 (52.4)	148 (48.5)
Age		
16 to <18 years	101 (29.7)	–
12 to <16 years	239 (70.3)	–
Race		
American Indian or Alaska Native	0	3 (1.0)
Asian	15 (4.4)	30 (9.8)
Black or African American	4 (1.2)	34 (11.1)
Native Hawaiian or Other Pacific Islander	0	2 (0.7)
White	285 (83.8)	211 (69.2)
Other	7 (2.1)	8 (2.6)
Multiracial	19 (5.6)	14 (4.6)
Not reported	6 (1.8)	3 (1.0)
Unknown	4 (1.2)	0
Ethnicity		
Hispanic or Latino	26 (7.6)	81 (26.6)
Not Hispanic or Latino	304 (89.4)	222 (72.8)
Not reported	9 (2.6)	0
Unknown	1 (0.3)	2 (0.7)
Race and ethnicity group*		
White non-Hispanic	267 (78.5)	147 (48.2)
Communities of color	69 (20.3)	158 (51.8)
Missing	4 (1.2)	0
Body mass index		
<30 kg/m^2	316 (92.9)	233 (76.4)
≥30 kg/m^2	24 (7.1)	71 (23.3)
Positive baseline SARS-CoV-2 status†	0	0
Negative baseline SARS-CoV-2 status‡	340 (100)	305 (100)

Legend: Covid-19 = coronavirus disease 2019; RT-PCR = reverse transcription polymerase chain reaction; SARS-CoV-2 = severe acute respiratory syndrome coronavirus-2. Percentages are based on the number of participants in the Immunogenicity Subset (N).

* White non-Hispanic is defined as White and non-Hispanic, and Communities of Color includes all the others whose race or ethnicity is not unknown, unreported, or missing.

† Positive if there is immunologic or virologic evidence of prior COVID-19, defined as positive RT-PCR test or positive Elecsys result at Day 1.

‡ Negative is defined as a negative RT-PCR test and negative Elecsys result at Day 1.

Table S11: Asymptomatic Infections 14 Days after the First Dose (mITT1 Set)

	Placebo (n=1073)	mRNA-1273 (n=2163)	Total
Total asymptomatic infections	29	25	54
Positive by RT-PCR only*	20	14	34
Positive by nucleocapsid serology (Elecsys) only	15	15	30
By both RT-PCR and nucleocapsid serology	6	4	10

*Positive nasopharyngeal swab by reverse transcriptase-polymerase chain reaction for SARS-CoV-2

Table S12: Demographics of Adolescents (12-<18 years) Compared with Participants in the Phase 3 COVE Trial

Characteristic n (%)	Adolescents 12-<18 years N=3726	Phase 3 COVE Trial ≥18 years N=30351
Age (years)		
Mean	14.3	51.4
Gender		
Male	1915 (51)	15985 (53)
Female	1811 (49)	14366 (47)
Race		
White	3126 (84)	24024 (79)
Black or African-American	125 (3)	3090 (10)
Asian	221 (6)	1382 (5)
Native Hawaiian or Other Pacific Islander	2 (<1)	67 (<1)
American Indian or Alaska Native	19 (<1)	233 (<1)
Multiracial	168 (5)	636 (2)
Other	36 (1)	637 (2)
Not reported or unknown	29 (<1)	282 (<1)
Ethnicity		
Hispanic or Latino	432 (12)	6235 (21)
Not Hispanic or Latino	3264 (88)	23835 (79)
Not reported or Unknown	30 (<1)	281 (<1)
RT-PCR results at baseline		
Positive	22 (<1)	182 (<1)
Negative	3447 (93)	29840 (98)
Missing	257 (7)	329 (1)
Serology result against nucleocapsid antigen at baseline		
Positive	202 (5)	608 (2)
Negative	3452 (93)	29416 (97)
Missing	72 (2)	327 (1)
Positive baseline SARS-CoV-2 status*	216 (6)	680 (2)
Negative baseline SARS-CoV-2 status †	3242 (87)	29148 (96)
Missing baseline SARS-CoV-2 status	268 (7)	523 (2)

* Positive if there is immunologic or virologic evidence of prior Covid-19, defined as positive RT-PCR test or positive serology result for the nucleocapsid antigen (Elecsys) at Day 1.

† Negative is defined as a negative RT-PCR test and negative Elecsys serology result at Day 1. SD=standard deviation.

Table S13: Incidence of Solicited Adverse Reactions with Onset after Day 7 after any Injection

Adverse Reaction **n (%)**	**Placebo N=1240**	**mRNA-1273 N=2486**	**Total N=3726**
Number of Participants Reporting Solicited Adverse Reaction	4 (0.3)	47 (1.9)	51 (1.4)
Number of Participants Reporting Solicited Systemic Adverse Reaction	4 (0.3)	18 (0.7)	22 (0.6)
Number of Participants Reporting Solicited Local Adverse Reaction	0	32 (1.3)	32 (0.9)
Number of Solicited Adverse Reactions	7	81	88
Pain	0	6 (0.2)	6 (0.2)
Erythema	0	17 (0.7)	17 (0.5)
Swelling	0	11 (0.4)	11 (0.3)
Axillary Swelling	0	11 (0.4)	11 (0.3)
Fever	1 (<0.1)	4 (0.2)	5 (0.1)
Headache	2 (0.2)	7 (0.3)	9 (0.2)
Fatigue	2 (0.2)	8 (0.3)	10 (0.3)
Myalgia	0	4 (0.2)	4 (0.1)
Arthralgia	0	2 (<0.1)	2 (<0.1)
Nausea / vomiting	1 (<0.1)	4 (0.2)	5 (0.1)
Chills	1 (<0.1)	1 (<0.1)	2 (<0.1)
Percentages are based on the number of participants in the safety set.			